Code: p0794

Abstract: 340

Role of matrix metalloproteinase-9 (MMP-9), rho kinase (ROCK II) and glycogen synthase kinase-3β (GSK-3β) in the protective effect of curcumin in pentylenetetrazole (PTZ)-induced kindling in rats

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Purpose: We have recently demonstrated anti-epileptic effect of curcumin. Matrix metalloproteinase-9 (MMP-9), rho kinase (ROCK II) and glycogen synthase kinase-3-β (GSK-3β) have been implicated in pathogenesis of epilepsy. In the present study, the effect of curcumin on the expression of MMP-9, ROCK II and GSK-3β in pentylenetetrazole (PTZ)-induced kindling was evaluated.
Method: PTZ (30 mg/kg, i.p.) was administered on alternate days up to day 43 or until seizure stage 5 on two consecutive trials was achieved, whichever was earlier. Curcumin, suspended in 0.1 % carboxymethylcellulose (CMC), was administered daily per orally (p.o). The animals were randomly divided into 5 groups (n=6). Group I (Normal control) received no active treatment. Group II (vehicle control) was administered 0.9% saline i.p. and CMC p.o. Group III (PTZ group) was injected PTZ, i.p on alternate days. Group IV was pretreated with curcumin in a dose of 300 mg/kg in addition to alternate day PTZ. In this group, curcumin was administered 30 min before PTZ administration on the days of PTZ injection. Group V (*per se*) was administered curcumin, 300 mg/kg, p.o daily. Western blot analysis was performed to study the expression of MMP-9, ROCK II and GSK-3β.
Results: Curcumin caused significant increase in development of kindling, latency to myoclonic jerks as well as latency to GTCS and decrease in number of myoclonic jerks as compared to PTZ group. PTZ-induced kindling in rats caused significant increase in the expressions of MMP-9, ROCK II and GSK -3β which were prevented by curcumin. Curcumin *per se* did not alter MMP-9, ROCK II and GSK -3β expressions.
Conclusion: This study demonstrates a possible role of MMP-9, ROCK II and GSK -3β in the antiepileptic effect of curcumin in PTZ-induced kindling in rats.
Acknowledgement: The work was supported by Institute Research Grant to Dr KH Reeta.

Code: p0795

Abstract: 1195

The protective effect of curcumin in a model of temporal lobe epilepsy in the rat via modification of Bax and Bcl2

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Purpose: Temporal lobe epilepsy is associated with apoptosis and neuronal degeneration in hippocampus. Curcumin (the main constituent of the medicinal plant *Curcuma longa*) has antioxidant and anticonvulsant activity, therefore, this study was conducted to assess its effect on Bax and Bcl2 positive hippocampal neurons in kainate-epileptic rats.
Method: In this study, 28 male rats were divided into sham, curcumin-pretreated sham, epileptic (kainate), and curcumin-pretreated epileptic groups. Experimental model of epilepsy was induced by unilateral intrahippocampal administration of 1 µg of kainic acid per rat. Rats received curcumin (100 mg/kg, p.o.) daily, started two days before surgery till 1 h pre-surgery. One day post-kainate injection, Bax and Bcl2 immunohistochemistry was conducted on hippocampal sections in addition to Nissl staining and behavioral assessment of seizure activity.
Results: Induction of epilepsy was followed by a significant seizure and curcumin pretreatment significantly reduced seizure intensity ($p< 0.01$). In addition, there was no significant difference between the groups in Nissl staining of CA3 area neurons. On the other hand, Bax positive neurons were observed in CA3 area in kainate group and curcumin pretreatment significantly lowered it ($p< 0.05$). Meanwhile, Bcl2 positive neurons were also moderately observed in kainate group and curcumin pretreatment significantly increased it ($p< 0.05$).
Conclusion: Curcumin pretreatment of epileptic rats exhibits anticonvulsant activity, decreases expression of proapoptotic protein Bax and significantly enhances expression of anti-apoptotic protein Bcl2 and this could reduce neuronal apoptosis.

Code: p0796

Abstract: 757

Upstream and downstream mTOR pathway hyperactivation in focal cortical dysplasia type II

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Purpose: FCD II are malformation of cortical development frequently associated with intractable epilepsy and characterized by cortical dyslamination and abnormal cells including dysmorphic neurons (DNs) and balloons (BCs). The downstream mediators of the mTOR pathway - important network involved in multiple functions during development and maturational stages - are abnormally activated in both DNs and BCs, suggesting a role in the pathogenesis of FCD II, but less is known about upstream activators. Aim of this work is to clarify the contribution of the upstream compartment PI3K-Akt to mTOR pathway activation in surgical specimens presenting FCD II.
Method: We analyzes, in surgical samples from patients with FCD II (19 cases) and Rasmussen Encephalitis (RE- 3 cases used as comparison tissue without developmental malformation), the expression pattern of pS6 (downstream target), pPDK1 and pAkt (upstream targets). We also perform a cell count and a plotting analysis of BCs and DNs positive for mTOR markers. Moreover, immunofluorescence experiments were made combining mTOR markers with GAD, VIM and SMI (to identify interneurons, BCs and DNs).
Results: In FCD II, DNs and BCs express upstream and downstream targets. pS6 is detected in almost all abnormal cells, conversely, pPDK1 and pAkt, distributed in the same spatial areas of pS6, are observed in a less proportion of DNs (respectively in 41% and 25%) and BCs (respectively in 87% and 63 %). In contrast, in RE cases, the rare DNs are pS6 positive but pPDK1 and pAkt negative.
Conclusion: In FCD II, the PI3K-Akt compartment is only partially responsible to the mTOR hyperactivation; therefore, as in acquired epilepsy (RE), additional mechanisms, for example linked to epileptic activity or inflammatory mechanisms might be involved.